

AMENDMENT

Kindly amend the application, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

IN THE CLAIMS:

Kindly amend the application, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, to read as follows:

1. (Currently Amended) A complex comprising an HLA class I molecule or fragment thereof, the HLA class I molecule or fragment thereof comprising: a T cell binding portion, and an attaching means for selectively attaching said HLA class I molecule or fragment thereof to a target cell, wherein the HLA class I molecule or fragment thereof binds or is attached to a recognition peptide, wherein the recognition peptide is arranged to be presented by said HLA class I molecule or fragment thereof for T cell recognition, wherein the attachment means comprises:

- a) a linking polypeptide with specific affinity for a molecule on the surface of the target cell; and
- b) a coupling system for coupling the linking polypeptide to the HLA class I molecule or fragment thereof, wherein the coupling system comprises:
 - (i) a first small molecule joined to the linking polypeptide; and
 - (ii) a second small molecule joined to the HLA class I molecule,

wherein the first and second small molecules are each selected from biotin and avidin/streptavidin or calmodulin and calmodulin binding peptides;

wherein interaction of the small molecules forms a stable bridge between the linking polypeptide and the HLA class I molecule.

- 2. (Cancelled)
- 3. (Previously Presented) The complex as claimed in claim 1, wherein said linking polypeptide comprises an antibody raised against said molecule on the surface of the target cell.
- 4. (Currently Amended) A complex comprising an HLA class I molecule or fragment thereof, the HLA class I molecule or fragment thereof comprising: a T cell binding

portion, and an attaching means for selectively attaching said HLA class I molecule or fragment thereof to a target cell, wherein said attaching means comprises a linking polypeptide which binds r is attached to said target cell and wherein said linking polypeptide is adapted to be attached directly to said HLA class I molecule or fragment thereof; and wherein the HLA class I molecule or fragment thereof additionally binds or is attached to a recognition peptide, wherein the recognition peptide is arranged to be presented by said HLA class I molecule or fragment thereof for T cell recognition, ~~wherein said linking polypeptide is adapted to be attached directly to said HLA class I molecule or fragment thereof.~~

5. (Cancelled)

6. (Cancelled) ~~The complex as claimed in claim 1, wherein said coupling system comprises a three-step chain of small molecules.~~

7. (Cancelled) ~~A complex comprising an HLA class I molecule or fragment thereof, the HLA class I molecule or fragment thereof comprising: a T cell binding portion, and an attaching means for selectively attaching said HLA class I molecule or fragment thereof to a target cell, wherein the HLA class I molecule or fragment thereof binds or is attached to a recognition peptide, wherein the recognition peptide is arranged to be presented by said HLA class I molecule or fragment thereof for T cell recognition, wherein the attachment means comprises:~~

~~a) a linking polypeptide with specific affinity for a molecule on the surface of the target cell; and~~

~~b) a coupling system for coupling the linking polypeptide to the HLA class I molecule or fragment thereof, wherein the coupling system comprises:~~

~~(i) — a first small molecule joined to the linking polypeptide; and~~

~~(ii) — a second small molecule joined to the HLA class I molecule,~~

~~wherein interaction of the small molecules forms a stable bridge between the linking polypeptide and the HLA class I molecule, wherein said coupling system comprises a three-step chain of small molecules, and wherein said chain comprises biotin and avidin/streptavidin.~~

8. (Cancelled) ~~A complex comprising an HLA class I molecule or fragment thereof, the HLA class I molecule or fragment thereof comprising: a T cell binding portion, and an attaching means for selectively attaching said HLA class I molecule or fragment thereof to a target cell, wherein the HLA class I molecule or fragment thereof binds or is attached to a~~

~~recognition peptide, wherein the recognition peptide is arranged to be presented by said HLA class I molecule or fragment thereof for T cell recognition, wherein the attachment means comprises:~~

- ~~a) a linking polypeptide with specific affinity for a molecule on the surface of the target cell; and~~
- ~~b) a coupling system for coupling the linking polypeptide to the HLA class I molecule or fragment thereof, wherein the coupling system comprises:
 - ~~(i) — a first small molecule joined to the linking polypeptide; and~~
 - ~~(ii) — a second small molecule joined to the HLA class I molecule;~~~~

~~wherein interaction of the small molecules forms a stable bridge between the linking polypeptide and the HLA class I molecule, wherein said coupling system comprises a three step chain of small molecules, and wherein said chain comprises calmodulin and calmodulin binding peptide.~~

9. (Previously Presented) The complex as claimed in claim 1, which complex comprises a recombinant protein, which recombinant protein includes a moiety comprising said HLA class I molecule or fragment thereof, and a moiety comprising said attaching means.

10. (Cancelled)

11. (Previously Presented) The complex as claimed in claim 1, wherein said target cell is a type of cell the presence of which is undesirable in a patient, selected from the group consisting of a tumour cell, a diseased cell, a foreign cell, a malignant cell, a leukaemia cell, an infected cell, or a cell responsible for detrimental activity in auto-immune disease.

12. (Currently Amended) The complex as claimed in claim 1, wherein the recognition peptide comprises a peptide which has a ~~strong~~ cytotoxic T cell response or which is capable of inducing an ~~powerful~~ immune response.

13. (Previously Presented) The complex as claimed in claim 1, wherein said recognition peptide comprises one or more of a tumour specific peptide, a viral peptide, a bacterial peptide, a parasitic peptide or microbial peptide.

14. (Previously Presented) The complex as claimed in claim 1, wherein the allotype of said HLA class I molecule or fragment thereof is different from the allotype of the HLA class I molecules of the patient, so that an alloreactive response can additionally or alternatively be triggered against said target cell.

15. (Withdrawn) The complex as claimed in claim 1, wherein said target cell is an antigen presenting cell.

16. (Previously Presented) A complex as claimed in claim 15, wherein there is a recognition peptide that comprises a tumour specific peptide, or a viral peptide, or a bacterial peptide, or a parasite peptide, or any peptide which is exclusively or characteristically presented by HLA class I molecules on the surface of diseased or malignant cells, or virally, bacterially, parasitically or microbially infected cells, or foreign cells, the presence of which is undesirable in a patient.

17. (Previously Presented) The complex as claimed in claim 1, wherein said target cell is a culture cell.

18. (Previously Presented) The complex as claimed in claim 1, wherein said target cell is a cell in the body of a patient.

19. (Withdrawn) A method for attaching the complex of claim 1 to said target cell, comprising the step of introducing to said target cell said HLA class I molecule or fragment thereof and said attaching means.

20. (Withdrawn) Use of the complex of claim 15 in the in vivo or ex vivo amplification of cytotoxic T cells with specificity for said recognition peptide.

21. (Withdrawn) A method for producing or enhancing an immunological response against a target cell, comprising the step of attaching the complex of claim 1 to said target cell by introducing to said target cell a HLA class I molecule or fragment thereof and attaching means.

22. (Withdrawn) A method for immunizing a patient against a disease or condition which is characterized by the presence in the patient's body of cells displaying said recognition peptide on the surface thereof; such as a tumour, or a malignant or auto-immune disease such as cancer or leukaemia, an infectious disease such as a viral infection such as HIV infection, a bacterial or microbial infection such as tuberculosis, or a parasitic infection such as malaria; comprising the step of administering to said patient an effective amount of the complex of claim 15.

23. (Withdrawn) A pharmaceutical composition for immunising a patient against a disease or condition which is characterised by the presence of diseased, malignant or foreign cells in the body of the patient, said pharmaceutical composition comprising a complex as claimed in claim 15 and an appropriate excipient or carrier.

24. (Withdrawn) A method of preparing the pharmaceutical composition of claim 23 comprising providing a target cell, producing the complex of claim 15 by selectively attaching an HLA class I molecule or fragment thereof to the target cell, and combining the complex of claim 15 with an excipient or carrier.

25. (Withdrawn) A method for the treatment of a disease or condition such as a tumour, or a malignant or auto-immune disease such as cancer or leukaemia, an infectious disease such as a viral infection such as HIV infection, a bacterial or microbial infection such as tuberculosis, or a parasitic infection such as malaria, comprising the step of administering to a patient in need thereof an effective amount of the complex of claim 11.

26. (Previously Presented) A pharmaceutical composition for treating a patient having a disease or condition characterised by the presence of diseased, foreign or malignant cells in the body of the patient, said pharmaceutical composition comprising a complex as claimed in claim 11 and an appropriate excipient or carrier.

27. (Previously Presented) A method of preparing the pharmaceutical composition of claim 26 comprising providing a target cell, producing the complex of claim 11 by selectively attaching an HLA class I molecule or fragment thereof to the target cell, and combining the complex of claim 11 with an excipient or carrier.

28. (Withdrawn) A pharmaceutical pack or kit comprising one or more containers containing one or more pharmaceutical composition claimed in claim 23 and written instructions for the administration of said composition or compositions to a patient.

29. (Currently Amended) A pharmaceutical pack or kit comprising one or more containers, each container having therein a containing one or more pharmaceutical composition as claimed in claim 26, and written instructions for the administration of said ~~compositions~~ composition to a patient.

30. (Withdrawn) The complex as claimed in claim 13, wherein said viral or microbial peptide is selected from the group consisting of an influenza virus peptide, a measles virus peptide, an Epstein-Barr virus peptide, a Cytomegalovirus peptide, and a tetanus toxoid peptide.

31. (Withdrawn) The complex as claimed in claim 30, wherein the Epstein-Barr virus peptide comprises the RAKFFQLL (SEQ ID NO:1) epitope of BZLF1 lytic protein.

32. (Previously presented) The pharmaceutical composition as claimed in claim 23 or 26, wherein the disease or condition is selected from the group consisting of a tumour, a

malignant or auto-immune disease, an infectious disease, a viral infection, a bacterial infection, and a parasitic infection.

33. (Previously presented) The pharmaceutical composition as claimed in claim 32, wherein the malignant disease is cancer or leukaemia.

34. (Withdrawn) The pharmaceutical composition as claimed in claim 32, wherein the viral infection is HIV.

35. (Withdrawn) The pharmaceutical composition as claimed in claim 32, wherein the bacterial infection is tuberculosis.

36. (Withdrawn) The pharmaceutical composition as claimed in claim 32, wherein the parasitic infection is malaria.

37. (Previously presented) The complex as claimed in claim 3, wherein the antibody is a monoclonal antibody.

38. (Withdrawn) The complex as claimed in claim 11, wherein the infected cell is infected with a parasite, bacterium, microbe or virus.

39. (Withdrawn) The complex as claimed in claim 38, wherein the virus is HIV.

40. (Withdrawn) A complex comprising

(i) an HLA class I molecule or a fragment thereof;

(ii) an attachment means comprising either

a) a molecule which specifically binds a polypeptide selected from the group consisting of carcinoembryonic antigen, placental alkaline phosphatase, polymorphic epithelial mucin, human chorionic gonadotrophin, CD20, prostate specific antigen, ca-125 and HMW-MAA; or

b) an antibody selected from the group consisting of C46, 85A12, H17E2, HMFG1, W14, 1F5, and 225.28s; and

(iii) a recognition peptide selected from the group consisting of an influenza virus peptide, a measles virus peptide, an Epstein-Barr virus peptide, a peptide comprising the RAKFFQLL epitope of BZLF1 lytic protein, a Cytomegalovirus peptide and a tetanus toxoid peptide;

wherein the recognition peptide is arranged to be presented by the HLA class I molecule or fragment thereof for T cell recognition.

41. (Withdrawn) The complex according to claim 40 further comprising a coupling system for joining the attachment means to the HLA molecule or fragment thereof.
42. (Withdrawn) The complex according to claim 41 wherein the coupling system comprises one or more of biotin, avidin, streptavidin, calmodulin or calmodulin binding protein.
43. (Withdrawn) A complex comprising
- (i) an HLA-A2 molecule or a fragment thereof, conjugated to biotin;
 - (ii) a monoclonal antibody 225.28s conjugated to biotin;
 - (iii) avidin; and
 - (iv) a peptide comprising the amino acid sequence SLYNTVATL (SEQ ID NO:2).
44. (Withdrawn) A pharmaceutical composition comprising
- (i) the complex according to claim 40 or 43, and
 - (ii) a pharmaceutically acceptable excipient or carrier.
45. (Withdrawn) A kit comprising one or more pharmaceutical compositions according to claim 44 and written instructions for the administration of said composition(s) to a subject.
46. (Currently Amended) A complex comprising an HLA class I molecule or fragment thereof, the HLA class I molecule or fragment thereof comprising: a T cell binding portion, and an attaching means for selectively attaching said HLA class I molecule or fragment thereof to a target cell, wherein the HLA class I molecule or fragment thereof binds or is attached to a recognition peptide, wherein the recognition peptide is arranged to be presented by said HLA class I molecule or fragment thereof for T cell recognition, wherein the attachment means comprises:
- a) a linking polypeptide with specific affinity for a molecule on the surface of the target cell; and
 - b) a coupling system for coupling the linking polypeptide to the HLA class I molecule or fragment thereof, wherein the coupling system consists essentially of:
 - (i) a first small molecule joined to the linking polypeptide; and
 - (ii) a second small molecule joined to the HLA class I molecule,
- wherein the first and second small molecules are each selected from biotin and avidin/streptavidin or calmodulin and calmodulin binding peptides;

wherein interaction of the small molecules forms a stable bridge between the linking polypeptide and the HLA class I molecule.

47. (Previously presented) The complex as claimed in claim 46, wherein said linking polypeptide comprises an antibody raised against said molecule on the surface of the target cell.

48. (Previously presented) The complex as claimed in claim 47, wherein the antibody is a monoclonal antibody.

49. (Cancelled) ~~A complex comprising an HLA class I molecule or fragment thereof, the HLA class I molecule or fragment thereof comprising: a T cell binding portion, and an attaching means for selectively attaching said HLA class I molecule or fragment thereof to a target cell, wherein the HLA class I molecule or fragment thereof binds or is attached to a recognition peptide, wherein the recognition peptide is arranged to be presented by said HLA class I molecule or fragment thereof for T cell recognition, wherein said linking polypeptide is adapted to be attached directly to said HLA class I molecule or fragment thereof.~~

50. (Previously Presented) A complex comprising an HLA class I molecule or fragment thereof, the HLA class I molecule or fragment thereof comprising: a T cell binding portion, and an attaching means for selectively attaching said HLA class I molecule or fragment thereof to a target cell, wherein the HLA class I molecule or fragment thereof binds or is attached to a recognition peptide, wherein the recognition peptide is arranged to be presented by said HLA class I molecule or fragment thereof for T cell recognition, wherein the attachment means comprises:

- a) a linking polypeptide with specific affinity for a molecule on the surface of the target cell; and
- b) a coupling system for coupling the linking polypeptide to the HLA class I molecule or fragment thereof, wherein the coupling system consists essentially of:
 - (i) a first small molecule joined to the linking polypeptide; and
 - (ii) a second small molecule joined to the HLA class I molecule,

wherein interaction of the small molecules forms a stable bridge between the linking polypeptide and the HLA class I molecule and wherein said coupling system consists of biotin and avidin/streptavidin.

51. (Previously Presented) A complex comprising an HLA class I molecule or fragment thereof, the HLA class I molecule or fragment thereof comprising: a T cell binding

portion, and an attaching means for selectively attaching said HLA class I molecule or fragment thereof to a target cell, wherein the HLA class I molecule or fragment thereof binds or is attached to a recognition peptide, wherein the recognition peptide is arranged to be presented by said HLA class I molecule or fragment thereof for T cell recognition, wherein the attachment means comprises:

- a.) a linking polypeptide with specific affinity for a molecule on the surface of the target cell; and
- b.) a coupling system for coupling the linking polypeptide to the HLA class I molecule or fragment thereof, wherein the coupling system consists essentially of:
 - (i) a first small molecule joined to the linking polypeptide; and
 - (ii) a second small molecule joined to the HLA class I molecule,

wherein interaction of the small molecules forms a stable bridge between the linking polypeptide and the HLA class I molecule and wherein said coupling system consists of calmodulin and calmodulin binding peptide.

52. (Previously presented) The complex as claimed in claim 46, which complex comprises a recombinant protein, which recombinant protein includes a moiety comprising said HLA class I molecule or fragment thereof, and a moiety comprising said attaching means.

53. (Previously presented) The complex as claimed in claim 46, wherein said target cell is a type of cell the presence of which is undesirable in a patient, selected from the group consisting of a tumour cell, a diseased cell, a foreign cell, or a malignant cell, a leukaemia cell, an infected cell, or a cell responsible for detrimental activity in auto-immune disease.

54. (Withdrawn) The complex as claimed in claim 53, wherein the infected cell is infected with a parasite, bacterium, microbe or virus.

55. (Withdrawn) The complex as claimed in claim 54, wherein the virus is HIV.

56. (Currently Amended) The complex as claimed in claim 46, wherein the recognition peptide comprises a peptide which has a ~~strong~~ cytotoxic T cell response or which is capable of inducing an ~~powerful~~ immune response.

57. (Previously presented) The complex as claimed in claim 46, wherein said recognition peptide comprises one or more of a tumour specific peptide, a viral peptide, a bacterial peptide, a parasitic peptide or microbial peptide.

58. (Withdrawn) The complex as claimed in claim 57, wherein said viral or microbial peptide is selected from the group consisting of an influenza virus peptide, a measles virus peptide, an Epstein-Barr virus peptide, a Cytomegalovirus peptide, and a tetanus toxoid peptide.

59. (Withdrawn) The complex as claimed in claim 58, wherein the Epstein-Barr virus peptide comprises the RAKFFQLL (SEQ ID NO:1) epitope of BZLF1 lytic protein.

60. (Previously presented) The complex as claimed in claim 46, wherein the allotype of said HLA class I molecule or fragment thereof is different from the allotype of the HLA class I molecules of the patient, so that an alloreactive response can additionally or alternatively be triggered against said target cell.

61. (Withdrawn) The complex as claimed in claim 46, wherein said target cell is an antigen presenting cell.

62. (Withdrawn) A complex as claimed in claim 61, wherein there is a recognition peptide that comprises a tumour specific peptide, or a viral peptide, or a bacterial peptide, or a parasite peptide, or any peptide which is exclusively or characteristically presented by HLA class I molecules on the surface of diseased or malignant cells, or virally, bacterially, parasitically or microbially infected cells, or foreign cells, the presence of which is undesirable in a patient.

63. (Previously presented) The complex as claimed in claim 46, wherein said target cell is a culture cell.

64. (Previously presented) The complex as claimed in claim 46, wherein said target cell is a cell in the body of a patient.

65. (Withdrawn) A pharmaceutical composition for use in immunising a patient against a disease or condition which is characterised by the presence of diseased, malignant or foreign cells in the body of the patient, said pharmaceutical composition comprising a complex as claimed in claim 61 and an appropriate excipient or carrier.

66. (Withdrawn) A method of preparing a pharmaceutical composition for use in immunising a patient against a disease or condition which is characterised by the presence of diseased, malignant or foreign cells in the body of the patient, said pharmaceutical composition comprising a complex as claimed in claim 61 and an appropriate excipient or carrier comprising providing a target cell, producing the complex of claim 61 by selectively attaching an HLA class I molecule or fragment thereof to the target cell, and combining the complex of claim 61 with an excipient or carrier.

67. (Previously presented) A pharmaceutical composition for treating a patient having a disease or condition characterised by the presence of diseased, foreign or malignant cells in the body of the patient, said pharmaceutical composition comprising a complex as claimed in claim 53 and an appropriate excipient or carrier.

68. (Previously Presented) A method of preparing a pharmaceutical composition for treating a patient having a disease or condition characterised by the presence of diseased, foreign or malignant cells in the body of the patient, said pharmaceutical composition comprising a complex as claimed in claim 53 and an appropriate excipient or carrier comprising providing a target cell, producing the complex of claim 53 by selectively attaching an HLA class I molecule or fragment thereof to the target cell, and combining the complex of claim 53 with an excipient or carrier.

69. (Previously presented) The pharmaceutical composition as claimed in claim 65 or 67, wherein the disease or condition is selected from the group consisting of a tumour, a malignant or auto-immune disease, an infectious disease, a viral infection, a bacterial infection, and a parasitic infection.

70. (Previously presented) The pharmaceutical composition as claimed in claim 69, wherein the malignant disease is cancer or leukaemia.

71. (Withdrawn) The pharmaceutical composition as claimed in claim 69, wherein the viral infection is HIV.

72. (Withdrawn) The pharmaceutical composition as claimed in claim 69, wherein the bacterial infection is tuberculosis.

73. (Withdrawn) The pharmaceutical composition as claimed in claim 69, wherein the parasitic infection is malaria.

74. (Withdrawn) A pharmaceutical pack or kit comprising one or more containers containing one or more pharmaceutical composition claimed in claim 65 and written instructions for the administration of said composition or compositions to a patient.

75. (Currently Amended) A pharmaceutical pack or kit comprising one or more containers, each container having therein a ~~containing one or more~~ pharmaceutical composition as claimed in claim 69, and written instructions for the administration of said ~~compositions~~ composition to a patient.